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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/672,876	09/25/2003	Stephen Donovan	17607 (BOT)	4618

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STEPHEN DONOVAN
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EXAMINER

KAM, CHIH MIN

ART UNIT	PAPER NUMBER
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1656

DATE MAILED: 11/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/672,876

Applicant(s)

DONOVAN, STEPHEN

Examiner

Chih-Min Kam

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 October 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5 and 13 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5 and 13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 9/25/03; 11/4/03; 9/24/05
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-5 and 13 in the response filed October 18, 2005 is acknowledged. In the response, claims 6-12 have been cancelled. The traversal is on the ground(s) that all of the claims encompass a botulinum toxin, thus a single search should suffice to search all the claims. The response has been considered, however, the argument is not found persuasive because coexamination of Groups II and III would require additional search for the composition and method steps unnecessary for the examination of the elected claims. Therefore, co-examination of each of these inventions would require a serious additional burden of search.

The restriction groups have acquired a separate status in the art as a separate subject for inventive effect and require independent searches. The search for each of the invention is not coextensive particularly with regard to the literature search. A reference which would anticipate the invention of one group would not necessarily anticipate or make obvious any of the other group. The literature search, particularly relevant in this art, is not co-extensive and is much more important in evaluating the burden of search. Burden in examining materially different groups having materially different issues also exist.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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2. Claims 1-2, 4, 5 and 13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for obtaining a biologically active botulinum toxin, comprising (a) providing a fermentation medium that is substantially free of an animal-based product and comprises a protein product of soybean, (b) culturing a clostridial botulinum bacterium in the fermentation medium under conditions permitting production of a botulinum toxin and (c) recovering a biologically active botulinum toxin from the fermentation medium; and a method for making a substantially animal product free pharmaceutical composition comprising a botulinum toxin, the method comprising the steps of obtaining a biologically active botulinum toxin, and formulating the botulinum toxin, with a suitable excipient, does not reasonably provide enablement for a method for obtaining a biologically active botulinum toxin, and a method for making a substantially animal product free pharmaceutical composition comprising a botulinum toxin by using a fermentation medium that is substantially free of an animal derived product but without indicating a protein product that replaces animal-based products in the fermentation medium. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1-2, 4, 5 and 13 are directed to a method for obtaining a biologically active botulinum toxin, and a method for making a substantially animal product free pharmaceutical composition comprising a botulinum toxin by using a fermentation medium that is substantially free of an animal derived product. The specification, however, only discloses cursory conclusions without data supporting the findings, which states that the present invention provides media and processes which are free or substantially free of animal products, such as animal

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derived proteins, for obtaining or producing a biologically active botulinum toxin, and the botulinum toxin obtained can be used to make botulinum toxin as an active ingredient in pharmaceutical compositions. (page 14, lines 3-7). There are no indicia that the present application enables the full scope in view of a method of obtaining a biologically active botulinum toxin as discussed in the stated rejection. The present application does not provide sufficient teachings as to how the full scope of the claims is enabled. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breadth of the claims, the absence or presence of working examples, the state of the prior art and relative skill of those in the art, the predictability or unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breadth of the claims:

The breadth of the claims is broad and encompasses unspecified variants regarding the fermentation medium that is substantially free of an animal derived product, but without indicating a protein product that replaces animal-based products, which are not adequately described or demonstrated in the specification.

(2). The absence or presence of working examples:

Example 3 illustrates preparation of an animal product free fermentation media for clostridial botulinum; Example 4 illustrates growth of clostridium botulinum in an animal product free fermentation medium using a soy product; and Example 5 indicates determination of botulinum toxin production by clostridial botulinum grown in an animal product free

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fermentation medium. However, the specification has not demonstrated the use of other protein products aside from soy products to replace animal-based product in the fermentation medium.

(3). The state of the prior art and relative skill of those in the art:

The related art (e.g., USPN 6,558,926) indicates a system for the growth of *clostridial tetani* and production of tetanus toxin for use in the pharmaceutical composition, where the system includes growth media that contain significantly reduced levels of meat or dairy by-products using non-animal based products to replace the animal-based products (page 13, lines 13-21). However, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on the use of various protein products other than soy proteins to replace animal-based product in the fermentation medium, to be considered enabling for the claimed method associated with the variants.

(4). Predictability or unpredictability of the art:

The specification has shown the use of soy product to replace animal-based product in the fermentation medium in the claim methods, however, the specification does not teach the use of various protein products other than soy proteins in the fermentation medium, thus the effects of various protein products in the fermentation medium are unpredictable.

(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to a method for obtaining a biologically active botulinum toxin, and a method for making a substantially animal product free pharmaceutical composition comprising a botulinum toxin by using a fermentation medium that is substantially free of an animal derived product. Examples 3-5 illustrate the preparation of an animal product free

fermentation media for clostridial botulinum; the growth of clostridium botulinum in an animal product free fermentation medium using a soy product; and determination of botulinum toxin production by clostridial botulinum grown in an animal product free fermentation medium. The specification has shown the use of a soy product to replace animal-based product in the fermentation medium for the claim methods. However, the specification has not demonstrated the use of various protein products other than soy proteins to replace animal-based product in the fermentation medium, and there is no working example demonstrating the effects of various protein products in the fermentation medium. Since the specification fails to provide sufficient teachings on the use and effects of various protein products to replace animal-based product in the fermentation medium for the claimed methods, it is necessary to carry out undue experimentation to identify the protein product that is effective in replacing animal-based product in the fermentation medium.

(6). Nature of the Invention

The scope of the claims encompasses a method for obtaining a biologically active botulinum toxin using a fermentation medium that is substantially free of an animal derived product, but the specification does not provide the sufficient teachings on the use and effects of protein products that can replace animal-based products in the claimed methods. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broad, the working example does not demonstrate the claimed methods in associated with variants, the effect of the protein product to replace animal-based product is unpredictable, and the teaching in the specification are limited,

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therefore, it is necessary to carry out undue experimentation to identify various protein products that can replace animal-based product in the fermentation medium for the claimed method.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-5 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-5 and 13 are indefinite because of the use of the term "a fermentation medium that is substantially free of an animal derived product". The term cited renders the claim indefinite, it is not clear how much of an animal derived product the fermentation medium contains as to "substantially free", is it 1%, 5% or 10%? The specification defines the term "substantially free" as a level of less than one percent by weight of the pharmaceutical composition (page 18, lines 5-6), however, a fermentation medium is not a pharmaceutical composition, thus it is not clear what the term means when it refers to a fermentation medium. It is also not clear what product the term "an animal derived product" refers to? Claims 2-5 are included in this rejection for being dependent on a rejected claim and not correcting the deficiency of the claim from which they depend.

4. Claim 2 and 3 are indefinite because of the use of the term "derived from". The term cited renders the claim indefinite, it is not clear how different is the derived protein product from the parent protein in the vegetable. Claim 3 is included in this rejection for being dependent on a

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rejected claim and not correcting the deficiency of the claim from which it depends. Use of the term "obtained from" is suggested.

Claim Rejections-Obviousness Type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 1-5 and 13 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9, 16 and 17 of co-pending application 11/072,050 (published as US 2005/0238668). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-5 and 13 in the instant application disclose a method for obtaining a biologically active botulinum toxin, comprising (a) providing a fermentation medium that is substantially free of an animal derived product, where the medium may comprise a protein product from soybean, (b) culturing a clostridial botulinum bacterium in the fermentation medium under conditions permitting production of a botulinum toxin and (c) recovering a biologically active botulinum toxin from the fermentation medium; and a method for making a substantially animal product free pharmaceutical composition comprising a botulinum toxin, the method comprising the steps of obtaining a biologically active botulinum toxin, and formulating the botulinum toxin, with a

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suitable excipient; and the specification teaches the concentration of Hy-Soy in the fermentation medium is approximately 10-100g/L (1-10% by weight; page 26, lines 26-30), and the pH is approximately 5.5 to 7.1. This is obvious variation in view of claims 1-9, 16 and 17 of the co-pending application which disclose a method for obtaining a biologically active botulinum toxin, comprising (a) providing a fermentation medium that is substantially free of an animal derived product, and comprises between about 4-8% by weight of a soy derivative, (b) fermenting a clostridial botulinum bacterium in the fermentation medium under conditions permitting production of a botulinum toxin, and (c) recovering a biologically active botulinum toxin from the fermentation medium; and a method for making a substantially animal product free pharmaceutical composition comprising a botulinum toxin, the method comprising the steps of obtaining a biologically active botulinum toxin, and formulating the botulinum toxin, with a suitable excipient. Both sets of claims cite a method for obtaining a biologically active botulinum toxin, and a method for making a substantially animal product free pharmaceutical composition comprising a botulinum toxin by using a fermentation medium that is substantially free of an animal derived product and comprises a soy derivative. Thus, claims 1-5 and 13 in the present application and claims 1-9, 16 and 17 in the co-pending application are obvious variations of a method for obtaining a biologically active botulinum toxin, and a method for making a substantially animal product free pharmaceutical composition comprising a botulinum toxin by using a fermentation medium that is substantially free of an animal derived product and comprises a soy derivative.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

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Conclusion

6. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Patent Examiner



CHIH-MIN KAM
PATENT EXAMINER

CMK

November 08, 2005